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In Memoriam

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(PLATE XXXVI.)

The Times of 12th February 1925 contained the announcement that "on 9th February at 13 Wilbury Villas, Hove, Professor E. E. Klein, M.D., F.R.S., formerly of Barts, died at the age of 80." He was buried two days later at the Hove cemetery.

There were many to whom this notice came as a surprise for nothing had been heard of Dr Klein for some years and it had not been realised that he was so old a man. He had been amongst us, however, for fifty-five years and in his time had played an important part both as investigator and teacher. He had, in a manner, largely helped to shape the trend of english bacteriological and sanitary research. It is not an easy thing to present a correct picture of Dr Klein because he had worked so long in England that almost all his early associates had passed away or had ceased to be active participators in the fray. Of the younger generation many had never seen him and knew but little of his work. To them he was only a name—a man who had once been a figurehead, away however in the shadowy past of last century.

My claims to write this notice rest on an acquaintance with him for a quarter of a century and from a study of his published work during thirty years. I have also during the last few months examined afresh all his published work for the purpose of this notice. In addition I have had the advantage of coming into touch with several men who knew and worked with him when he first came to England. This account of him is, however, in some respects incomplete as at all times he was a rather elusive personality and did his life work for the most part alone even although attached to a medical school for many years.

The ordinary events of his life can be shortly told. Emanuel Klein was born on 31st October 1844 at Osijek (Essek), the chief town of Slavonia situated on the right bank of the Drave about thirteen miles from its junction with the Danube. Although slavonic born he was not really a slav but an Austrian of the jewish race, but not of its religion. He told one of my informants that his father was a tanner of russian leather—probably in a small way of business; and as he died early the care of the family devolved on Emanuel then a boy of

about fourteen. He had evidently managed to get a good education for he was able to teach the classics and in this way was able to gain a little money for the support of his mother. Klein related that he was in London at the age of eighteen—probably in some tutorial capacity. Leaving Essek he journeyed by river all the way to Vienna where he entered as a medical student in the University and in due course obtained his medical degree. He worked in the laboratory of Brücke the physiologist and then passed to the Institute of Salomon Stricker (1834-1898) at that time professor of general and experimental pathology and the opponent of Cohnheim in the polemic on experimental keratitis in the seventies of last century. Stricker was then in his zenith. When I attended his course in Vienna in 1893 he was a prematurely old man and I learned nothing from him: the students used to rag him unmercifully and his class was a bear garden. Klein became Privat-docent in histology under Stricker, who at that time was bringing out his famous *Handbuch von den Geweben des Menschen und der Thiere* (Leipzig, 1871-73, 2 vols. pp. 1248), and having been one of Stricker's assistants for about four years he was sent to England to negotiate about the translation of the work which was being made for the New Sydenham Society by Henry Power. Every one who met him here was charmed by the affable manners of the tall young Austrian who was destined shortly to settle here for life.

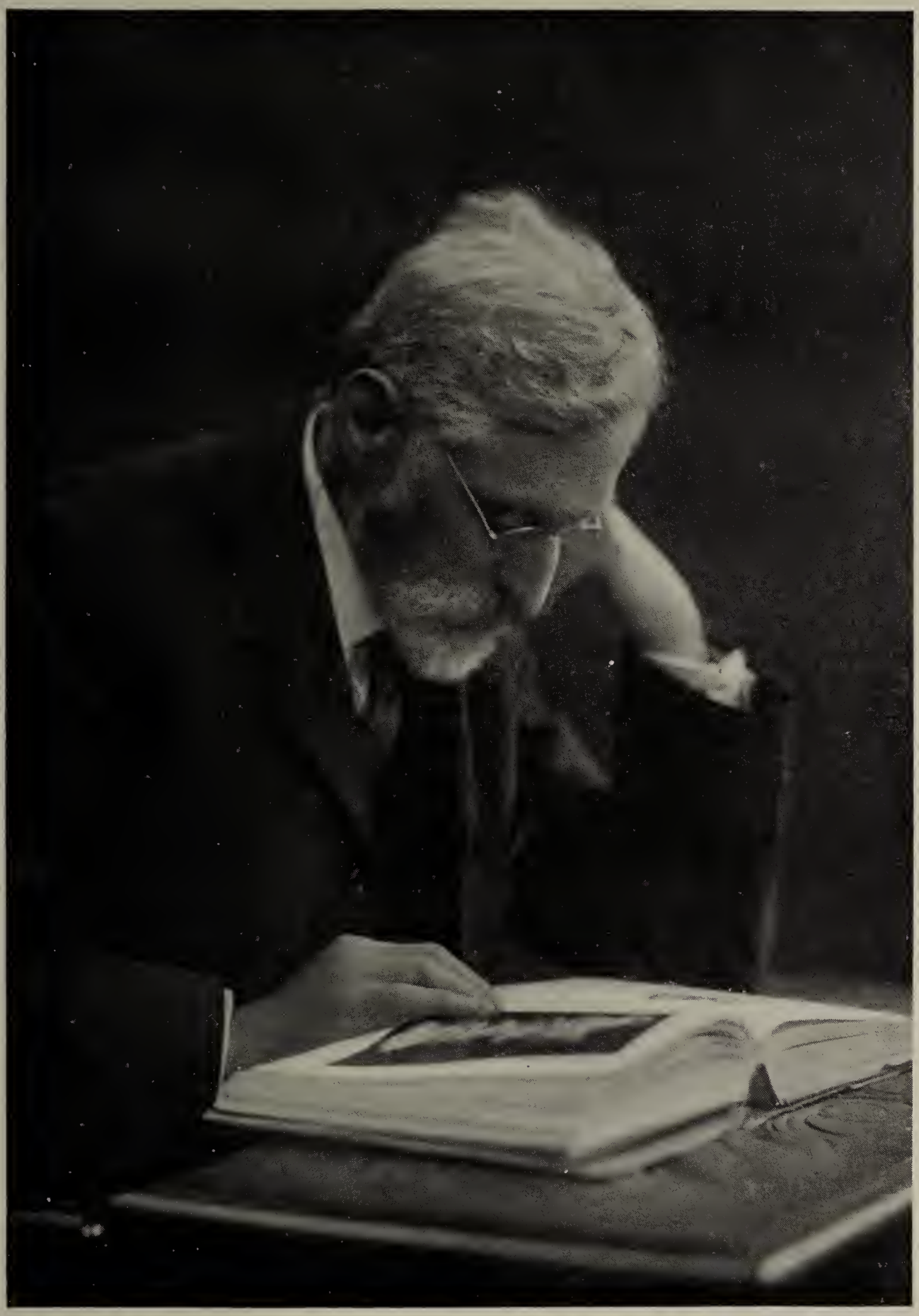
When the Brown Institution was founded in 1871 by the purchase of a piece of land with two houses in the Wandsworth Road, Burdon-Sanderson, the first superintendent, got Klein appointed on the recommendation of Ray Lankester, as the professor superintendent's scientific assistant, and he came to England early in 1872 and lived in one of the two above mentioned houses—now turned into shops. As assistant professor he received no payment. Indeed his early position at the Brown Institution was somewhat of an anomaly for at the Royal Commission on Vivisection in 1874 when asked the specific question (No. 3620) "What is your particular duty to the (London) University?" Klein replied, "I am ashamed to say I do not know; it has never been made clear to me."

The Brown Sanatory Institution has had a long and distinguished history but in some ways has now outlived its day. If one takes a tram from Westminster Bridge along the Embankment past Lambeth Palace and Doultons and underneath an ugly railway bridge across the Wandsworth Road one reaches (No. 149) a small archway on which is graven the legend "The Brown Sanatory Institution founded 1871." On entering, one comes to a stable yard and, behind, a low building of one storey. This is the famous "Brown" now falling, sad to say, into a considerable state of decay and uncared for. Here however have worked some of the foremost english medical scientists of a generation rapidly diminishing. The Brown is rarely visited and there must be many of the younger generation who know nothing about it nor what it stands for. To-day it is merely a name—a shadow of its former self. This queer derelict institution originated in a bequest by Mr Thomas Brown of Rosey Park Hill, Dublin (but a citizen of London), who died in 1852. He willed to the Chancellor,

Vice-Chancellor and Fellows of the University of London £20,000 and upwards for "founding, establishing and upholding an Institution for investigating, studying and, without charge beyond immediate expenses, endeavouring to cure maladies, distempers and injuries any quadrupeds or birds useful to man may be subject to, for and towards which purpose of founding, establishing and upholding such animal sanatory institution within a mile of either Westminster, Southwark or Dublin." Mr Brown also willed his other property, that the interest should accumulate for a term not exceeding fifteen years from the time of his death the money to go to the Animal Sanatory Institution. He directed that a Superintendent or Professor of the Institution should be appointed and should *have a residence adjacent to the Institution* and that he should give annually at least five lectures in english free to the public. "Kindness to animals shall be a general principle of the Institution" stated the will of Mr Brown.

Money being on the move it was not long before the validity of Mr Brown's bequest was contested by the next of kin mainly on the ground that such an Institution would not properly be a charity, but the University (of London) instituted a suit against the executors and the case was heard (1856) before the Master of the Rolls who decided that the bequest was a perfectly good gift. The University of Dublin appealed against the decision of the Master of the Rolls and the case was heard before the Lord Chancellor and the Lords of Appeal (1857) and they dismissed the appeal with costs as being thoroughly without foundation. In 1858 the "Brown" funds were transferred to the University of London and were allowed to accumulate until 1871 (19 years after Mr Brown's death) when the value of the stock was £33,781, 14s. 11d. Thereupon the Senate proceeded to execute the trust by establishing an Institution and appointed an administrative Committee and a professor superintendent viz. J. Burdon Sanderson. A question having arisen whether the Mortmain Act would allow any part of the Trust Fund to be applied to the purchase of land, the difficulty was got over by the gift of £2000 by Mr John Cunliffe of Lombard Street, and Burdon Sanderson himself added another £700. A site of about $1\frac{1}{2}$ acres was purchased in the Wandsworth Road and buildings were erected at a cost of £5000 and consisted of suitable stabling for horses, cows, sheep and pigs. A laboratory was also built and is still standing but somewhat dilapidated. It is a single large building with one floor of rooms above the ground level and a second, partly underneath it. The lower floor is reached from the upper by a trap door, still there, in the apparatus room. The whole Institution was opened late in 1871 (see *Lancet*, 1871, ii. 654). It was to this recently opened Institution that Klein was brought from Vienna to be the superintendent's Scientific Assistant. Burdon Sanderson (1828-1905) the first superintendent of the Brown had a long, distinguished and diversified career. For eleven years he had been Medical Officer of Health for Paddington and during part of this time he had also been Inspector for the Medical Department of the Privy Council under John Simon. He was also Assistant Physician (1859-1867) at the Brompton Hospital for Consumption, and Physician from 1867 till 1871. He also held an assistant physicianship at the Middlesex Hospital (1863-70) besides being in private practice up till 1870. He succeeded Foster as professor of practical physiology and histology at University College and when Sharpey retired in 1874 Sanderson was made Jodrell professor (1874-1883) with Schaefer as assistant. Every one knows that Burdon Sanderson migrated to Oxford as professor of physiology in 1882 and, finally, became Regius Professor of Medicine from 1895 till his death in 1905.

John Simon (1816-1904) pathologist and sanitary reformer was the first M.O.H. for the city of London (1848-1855) M.O. to the Board of Health from



E. Klebs.

1855 to 1858, M.O. to the Privy Council 1858-1876 and to the Local Government Board from 1871-1876. The Local Government Board was brought into existence as a result of the Act of 1871 and in 1870, under Mr Lowe's Chancellorship of the Exchequer, parliament approved the auxiliary scientific investigations as a separate item in the departmental estimate and began to grant an annual subsidy of £2000 a year which was first separately voted in 1871 and was the first national contribution to the world-wide interests of medical research (see Simon's *English Sanitary Institutions*, 1890).

There was a close co-operation between Simon and Burdon Sanderson who was working for the Privy Council on infective processes particularly in animals. When therefore the Brown legal troubles were at an end, Klein who was Sanderson's scientific assistant and who complied with the Brown Trust by residing on the premises at the Brown Institution really came under the ægis of Simon and the Privy Council and was paid from Mr Lowe's grant. Whether his emoluments were in the form of a fixed salary or for work done is not clear. At any rate Klein worked at the Brown and had charge of the laboratory which was "established, as part of the Institution, for the scientific study of the diseases of animals and . . . for researches into the action of remedies."

Klein was well received and was a *persona grata* from the start. A number of young consultants used to forgather at his house in Wandsworth Road to discuss science and incidentally to play whist. Joseph Frank Payne, Cavafy and Pye-Smith are known to have been members of the band. Klein was also permitted to have private pupils among whom were Francis Darwin, Jeremiah MacCarthy, James Adams and Frederick Treves.

Klein worked at the Brown from 1871 till 1897. By way of completeness I may add the Brown has had as its superintendents Burdon Sanderson (1871-1878), W. S. Greenfield (1878-1881), C. S. Roy (1881-1884), Victor Horsley (1884-1891), C. S. Sherrington (1891-1895), J. Rose Bradford (1895-1903), T. G. Brodie (1903-1909) and F. W. Twort (1909-). In addition to these there were private workers among whom may be recalled Charles Creighton, Wooldridge, W. G. Spencer, Ballance, Edmunds, Makins, A. E. Wright, Plimmer and E. Mellanby.

Klein was originally called Emanuel but usually signed himself "E" only, and through an accident came to be called Edward, which name he often used subsequently. The accident arose in this way that he was put up for membership for the Organon Club, and Corfield the hygienist and secretary of the club thinking that "E" stood for Edward, entered him as such, and so he was afterwards often called "Edward Emanuel." The "Organon" was founded by Ray Lankester and was a dining club of young medicos and scientists which met in London in the winter and in some place near by in summer.

In 1872 Morrant Baker, the surgeon, who was lecturer on physiology at St Bartholomew's Hospital invited Klein to give a course of eight demonstrations on histology at his hospital and he began, in this way, his long association with "Barts" where he became successively lecturer on histology (1872-1884), lecturer on general anatomy and physiology (1884-1900) and lecturer on advanced bacteriology (1903-1911). He retired with the title of Emeritus Lecturer. During all these years he was also a scientific medical worker for the Local Government Board in whose service almost all his bacteriological work was done. In 1875 Klein was elected F.R.S. (on the same day as Ray Lankester).

Before the Royal Commission on Vivisection in 1876 Klein made a rather unfortunate appearance which was probably due as he himself alleged to his defective knowledge of the subtleties of the english language. This defect was never totally overcome, for many years later I heard him use the word "prolifer" as a verb. The trouble with the Commission was that on being asked the question (No. 3539) "Do you mean that you have no regard at all for the sufferings of animals?" he gave the answer "no regard at all." He probably never meant this in the way that it sounds to us as he was known throughout life to be a great lover of animals, especially dogs. When the proof of his evidence was sent to him he altered it in some way, now obscure, but the Commission held that the alteration was at variance with the letter and spirit of the answers he gave at his examination and were unable to receive his emendation as an authentic report of his evidence. In consequence thereof Klein requested permission to withdraw his evidence altogether.

In 1885 he was sent to India in company with Heneage Gibbes and Alfred Lingard to study cholera and he was away for six months, which was long enough for him to disagree with Koch's conclusions which had at that time created a great stir. Klein came to the conclusion that the comma bacillus had not been proved to be the cause of asiatic cholera and he continued to hold this opinion for a number of years. In 1889 Klein was professor of bacteriology in the College of State Medicine, a venture which was established in 1886 and inaugurated in 1888. Its object was "to aid the theoretical and practical investigations and study of sanitary science and of all matters related thereto." The founders who were mostly retired surgeon-generals of the Navy, Army and Indian Services had it in mind to found a school on the model of Netley. A limited liability company without share capital was formed and the so-called college began its career in a small way in a couple of rooms in King William Street (Strand). In 1889 it was very generously assisted by the trustees of the estate of Richard Berridge who, dying in 1887, left a large sum of money to be applied to sanitary and social education. With money from the Berridge Trust the College of

State Medicine migrated to the house 101 Great Russell Street, W.C., which was adapted for its use at a cost of £800. Here Klein gave courses in bacteriology from 1888 till 1891 when he resigned and was succeeded by Allan Macfadyen. The College was never a flourishing proposition financially and in spite of further help from the Berridge Trust passed into liquidation in 1893 when it amalgamated with the British Institute of Preventive Medicine (now Lister Institute) and was accordingly wound up.

Klein was one of the original founders of the Medical Research Club (1891) and gave the first Horace Dobell lecture at the Royal College of Physicians in 1904. From 1877 till 1892 he was also joint editor of the *Quarterly Journal of Microscopical Science.*

Almost all Klein's early work was on *normal histology* a branch in which he was and remains an undoubted master. This was his early love and long after he had begun to tread the pathological path we find him returning again and again with vigour and freshness to the most diverse histological subjects. His first published paper (1868) was on the epithelium of the mucous membrane and the glands on the soft palate and uvula of man. For Stricker's *Handbuch* which appeared between 1871 and 1873 he wrote the articles on the thymus gland, external generative organs, the serous membranes, in conjunction with Verson the histology of the intestinal canal and, with Stricker and Stieda, the structure of the conjunctiva and sclerotic. In 1873 Klein wrote the histology section in the *Handbook for the Physiological Laboratory* a work edited by Burdon Sanderson, Foster, Brunton and Klein. In the same year he published an authoritative work under the rather unhappy title of *The Anatomy of the Lymphatic System* This was in two parts the first of which dealt with the normal and pathological condition of the serous membranes. He exploited with great success the method of silver impregnation of endothelium which had been introduced into histological technique in 1860 by von Recklinghausen, who demonstrated the continuity of the serous membranes with the lymphatic system. Besides the endothelium Klein dealt with the cellular elements of the ground substance and the lymph and blood vessels of normal serous membranes. The same tissues were considered in their pathological aspects especially as to the results of inflammation induced by ammonia iodine and toxic pyæmic fluids or tuberculous matter. In the production of the lesions Klein attributed great importance to the "germination of the endothelium," a change which had been previously described by Ranvier and Kundrat. In the second part of the *Anatomy of the Lymphatic System* (1875) Klein treated of the lung under normal and abnormal conditions. He gave a very minute account of this organ in the guinea-pig and studied in particular the changes wrought in tuberculosis. These works were undertaken for the Privy Council and were profusely illustrated with beautiful plates drawn by Klein from his own preparations. Between

1871 and 1884 Klein published twenty-seven papers on histological subjects chiefly in the *Quarterly Journ. of Micr. Science* but also in other journals such as the *Centralbl. f. d. med. Wissenschaft.* These papers cover a very wide area and include such subjects as non-medullated fibres (1871, 1872) Remak's ciliated vesicles in the peritoneum of the frog (1872) Auerbach's plexus (1873) development of the trout (1876) the omentum (1877) structure and division of cells (1878, 1879) spermatozoa (1880) corneal nerves (1880) nasal mucosa (1881) organ of Jacobson (1880-1882) lymphatics of the skin (1880) and salivary glands and pancreas (1882). With Langley and Schaefer he described (1884) the structure of the cortical areas removed from the brain of a dog and a monkey.

Klein's reputation as a histologist was greatly enhanced by the publication with the orthopedic surgeon Eldred Noble Smith (1847-1906) of the *Atlas of Histology* (1880). The forty-eight magnificent plates in this work were drawn by Noble Smith from Klein's preparations and many of them have been copied into most english works on anatomy and histology ever since. The Atlas is now a classic. Klein also wrote (1883) a standard work *Elements of Histology* which long had a most successful career in this country and was translated into French and German.

I have dealt at some length with Klein's activities as a histologist because it is very probable that he will be remembered longest by this work, notwithstanding that a large part of his life was spent in the pursuit of bacteriology and pathology. Before he came to this country Klein's work had been entirely of a histological character. He was brought to this country not, primarily, to do normal histology but really to comply with the requirements of the laboratory of the Brown Institution which was for the scientific study of the diseases of animals. At the time he was not trained for such work and it must be pointed out that although Burdon Sanderson had worked at experimental pathological questions the incursion of this physiologist into the study of infection cannot be described as fortunate when his work is read to-day.

On his arrival in England Klein was set to work at a very difficult—to-day still unsolved—problem viz. the nature of the contagion of *variola ovina* or sheep-pox. Ovine virus was obtained from Chauveau and from Ferdinand Cohn, and Klein inoculated sheep at the Brown Institution. The animals were kept in the basement near the fume chamber (still there) and communication with the laboratory above was by a trap door. Out of curiosity I descended through this trap on 6th March 1925 into a room of cimmerian darkness and hung with cobwebs that were ancient and heavy. It manifestly had never been the place for bacteriological researches and it is but little wonder that Klein did not find the contagion of ovine. He found indeed what he believed to be a mycelial fungus with gonidia in the variolous

skin and published the result in the *Proceedings of the Royal Soc.* (1874, xxii. 388) but had to withdraw it for Charles Creighton, a worker in the Brown at that time, found the same "fungus" in normal tissues hardened in chromic acid and spirit. Klein ultimately agreed that the mycelial fungus of ovine was due to coagulation of some substances connected with the blood. In withdrawing the fungoid theory of ovine Klein did a fine thing, for did not Lister say that "next to promulgation of new truth the best thing I conceive that a man can do is the recantation of published error."

About this time Klein was also working at the changes in enteric fever and here also he found what he thought was the *contagium vivum*, to use the language of that time, but this likewise was soon known to be incorrect. These first excursions of Klein into the experimental pathology of infection were fraught with disappointment but perhaps he was not altogether to blame. Not only was he not trained for such work by years of patient and disconcerting toil but in the early seventies bacteriology and its methods were at the best crude or almost non-existent. It was in a constant state of upheaval bordering on chaos. It may be of interest to define by a few landmarks the position of bacteriology when Klein began his pathological work in 1872.

It was in 1836 that Cagniard-Latour discovered that yeast was composed of living cells reproducing by budding. A year later Theodor Schwann showed that while no yeast cells are present in fresh grape juice the addition of leaven determines fermentation and gas production. The significance of the air still remained in question although the doctrine of fermentation and living organisms was gradually accepted. In 1840 Henle, with great prevision, gave a more definite meaning to the doctrine of *contagium vivum* as explaining infective diseases. He considered that, although invisible, contagia must be living and characterised by all the attributes that the older naturalists like Buffon and Spallanzani called "animality." Contagia, according to Henle, grow and multiply; they are capable of being transmitted from one individual to another and behave like parasites. Even before Henle, Agostino Bassi (1773-1856) had shown in 1835 that the silk-worm disease "calcino" or "muscardine" was due to the parasitic invasion of a well-defined fungus subsequently named *Botrytis bassiana*. Bassi's discovery soon led to the search for similar fungi in human diseases and resulted in the discovery of *Achorion Schoenleinii* (1839) thrush fungus (1841) and *Microsporon Audouini* (1844). Subsequent attempts to connect fungi with internal diseases were less happy and led to great confusion. At that time bacteria as we understand them to-day were regarded as curiosities for the microscope. Pasteur's first work on specific fermentation dates from 1857 when he studied the lactic change and he continued these investigations until interrupted by the revival in the doctrine of spontaneous generation which occurred through the publication of F. A. Pouchet's treatise *Hétérogénie* in 1859. This book led to Pasteur's classical experiments and the appearance of his great "mémoire sur les corpuscles organisés qui existent dans l'atmosphere" (*Ann. de chimie et de physique*, 1862, lxiv.). Of this work Tyndall wrote: "Clearness, strength and caution with consummate skill for their minister were rarely more strikingly displayed than in this imperishable essay." Although the opinion of Pasteur was that heterogenesis was not proven the heterogenists headed by Charlton Bastian made another attempt to instal the doctrine of

spontaneous generation in scientific literature and it was in 1872 that he published his *Beginnings of Life*, a work of more than 1000 pages. This led to acrimonious discussions in which Bastian was involved to the end of his life (1915). His experiments were plausible but his technique was shown to be very defective—although he remained unconvinced to the end.

While these discussions were going on the doctrine of *contagium vivum* was making slow and erratic progress. The great cholera pandemic of 1866 was a new incentive to activity and in particular Ernst Hallier, professor of botany in Jena, became a supporter of the view that infectious diseases were caused by living agents. He held however that the various micro-organisms were only special forms of moulds arising under the influence of extrinsic conditions. By a primitive and, as is now known, hopelessly defective apparatus he isolated and cultivated fungi from scarlet fever, measles, cholera, typhoid and other diseases. For a time his publications gained him a great notoriety until the eminent mycologist De Bary (1868) showed that his work was conducted with totally inadequate precautions against aerial contaminations. Indeed De Bary urged that Hallier's work was barren of all but mischievous results and was the more calculated to repel earnest observers because for a time it attracted some measure of success.

The downfall of Hallier's work may be looked upon as bringing to an ignominious end the first serious attempt to introduce the doctrine of *contagium vivum* as an ætiological factor in disease. The doctrine was however not killed outright but survived to burst forth anew and this time with success. From 1870 to 1874 a large number of observers among whom may be mentioned Coze and Feltz, von Recklinghausen, Waldeyer, Hueter, Birch-Hirschfeld, Lister, Burdon Sanderson and Klebs were successful in demonstrating, in wounds and abscesses, bodies that were far smaller than moulds and these were regarded as microbes. Klebs, in particular, showed the existence of a parasite in gun-shot wounds and their pyæmic sequelæ and named it *Microsporon septicum*. It was believed to be composed of mycelial threads associated with bacteria and rounded masses or zooglœa. At that time Nägeli's doctrine was that there were no species among bacteria, which were regarded as pleomorphic or protean.

Such was the state of knowledge when Klein began to investigate the ætiology of infective diseases in 1872, so that he was really in the same slough of despond as investigators elsewhere. The methods of staining were unknown. It was only in 1875 that Weigert taught us how to colour bacteria with hæmatoxylin or anilin dyes. C. J. Salomonsen (1876) and Koch (1877) followed closely in his track.

In 1872 Ferdinand Cohn (1828-1898) the Breslau botanist published the first part of his now classic "Untersuchungen über Bacterien" in his *Beiträge zur Biologie der Pflanzen* (1875, I. Heft 2, p. 167). In this research which is fundamental for all our subsequent knowledge he established as far as it was possible in the absence of pure cultivations that bacteria show constancy of form and specific differences among each other. The whole modern superstructure of bacteriology has been erected on this foundation. Cohn worked out a more or less satisfactory classification of bacteria, investigating their life history their nutritive requirements and the distinction between saprophytic and pathogenic microbes. In a second paper he gave an accurate account of bacterial spores and in a third he carried out experiments on their destruction by heat. His results led him to range himself alongside Pasteur and against the heterogenists. These papers of Cohn will well repay close study to-day and may prove a revelation to those whose knowledge of

bacteriology is bounded by the boards of a modern text book. Cohn's views derived great support from the work of his assistant J. Schroeter who in the same year (1872) published a most accurate account of chromogenic bacteria and their artificial cultivation on solid media like potato and bread paste.

The view of Cohn and Schroeter that species exist among bacteria as among other living things may be said to have been the real starting point of the quest for methods by which bacteria could be cultivated in a pure state.

From the first primitive attempts to the perfected technique of Koch a period of thirteen years elapsed viz. 1870-1883. It is true that Pasteur grew bacteria in fluids in 1857 but it has not been claimed that these growths were pure in the modern sense—indeed Koch threw considerable doubts on the purity of Pasteur's later cultures of anthrax. The methods of bacterial pure cultivation are divisible into great groups. In point of time the first methods were attempts to grow the micro-organisms in *transparent fluid* media. This began with Pasteur's fluid (1857) which was altered and perfected by Cohn in 1872. Fluids of this kind were mostly solutions of salts and of relatively simple constitution. More complicated nutritive fluids were devised by Nägeli and Miquel. The basic peptonised bouillon medium used everywhere to-day was first brought out by Loeffler in 1881 (*Mitth. a. d. Kais. Gsndhtsamt* Bd. i. p. 169). Media that were *solid* and *non-transparent* were used by Schroeter (1872) for chromogenic microbes. His potato, starch, white bread, egg albumen and flesh media while excellent for these bacteria were, however, much less useful for the non-pigmented types. In his early work Koch favoured potato media and greatly improved the technique for their preparation. Klebs in 1873 began to use gelatine or isinglass media for the purpose of what were called fractional cultures. Small quantities or fractions of the material to be cultivated were diluted down with an indifferent fluid so as to reach a quantity in which presumably only one microbe was present. This quantity was then added to an isinglass medium in a Recklinghausen-Geissler chamber and examined microscopically over a considerable period. Gelatine was primarily used to prevent evaporation which was very apt to occur with aqueous solutions. It had previously been used according to De Bary by Vittadini as far back as 1852, and it was also employed by Brefeld (1872) in his classical work on the cultivation of moulds. Brefeld strongly emphasised the importance of starting with one germ in order to obtain pure cultures. This was first done with success in the case of bacteria by Lister (1877) who isolated a pure culture of a lactic acid bacillus by growing it in sterile milk from a single bacterial cell obtained by a long series of dilutions made with a finely graduated syringe. He had however many previous failures before he succeeded with his method.

Although these methods represented an advance they were really so impracticable that many including Nägeli as late as 1877 declared that pure cultures were an impossibility. Salomonsen in his *Smaa Arbeijder* (1917, p. 272) relates that on a visit to Virchow the master on discussing pure bacterial cultures with him said in a laughing tone "'um ganz sicher zu gehen müsse man eigentlich für jede species ein besonderes kleines Laboratorium haben," indicating that he at any rate considered it was a very difficult task.

All the confusion however began to clear and the bacteriology of the pathogenic species may be said to date from the publication of Koch's paper in 1876 in Cohn's *Beiträge* (Bd. II. Heft 2, 277-310). It was entitled "Die Aetiologie der Milzbrand-krankheit begründet auf die Entwicklungsgeschichte des *Bacillus anthracis*." In this classic, Koch, then an unknown young "Kreisphysikus," described the complete life history of the anthrax bacillus and the formation, germination and significance of the anthrax spore. Cultures of bacteria constant in form were obtained in hanging drops of aqueous humour

or blood serum incubated in absurdly primitive apparatus composed of plates filled with wet sand. Koch showed that the anthrax bacillus never becomes converted into any other micro-organism and that it was pathogenic and produced nothing but anthrax when inoculated from one mouse to another even to the twentieth generation. *Bacillus subtilis* was incapable of producing anthrax. "Es folgt" says Koch (*loc. cit.* p. 298) "dass nur ein Bacillusart im Stande ist diesen specifischen Krankheitsprocess zu veranlassen während andere Schizophyten durch Impfung gar nicht oder in anderer Weise Krankheits-erregend wirken." This was the first time that the specificity of a pathogenic microbe had been definitely established. The date was 1876. The purification of a culture by inoculating susceptible animals has been frequently employed since Koch's anthrax paper was published. It is still the method of preserving pathogenic otherwise uncultivable viruses, such as those of rabies, vaccinia, swine fever, foot-and-mouth disease and rinderpest.

In the same year (1876) that Koch's anthrax work appeared C. J. Salomonsen obtained pure cultures of bacteria growing in putrid blood. He used very long capillary glass tubes and showed that specks—we should now call them colonies —appeared of varying size and shape. On examination, each speck was found to be composed of only one kind of bacterium. The method was not found to be applicable to fluids other than blood and now possesses only historic interest.

In 1881 a great advance was made by Koch in his invention of nutrient gelatine as a solid transparent culture medium. The gelatine united the advantages of solid media for separating bacteria with transparency for studying the result. Loeffler's nutrient broth was used as the basis and to this the gelatine was added, and the whole in a warm liquid state was poured on microscope slides. As the gelatine was setting Koch "inoculated" it by means of a platinum wire charged with the material to be cultivated. As the gelatine set the bacteria became fixed and as they grew later on they showed separate colonies the examination of which showed that each was composed of one type only of bacteria and in that sense was a "pure cultivation."

Koch demonstrated his method and results to a small but select audience including Pasteur in Lister's room at King's College, London, during the International Medical Congress in 1881. Lord Lister told me once that on seeing Koch's plate cultures Pasteur turned to him and said in a moment "C'est un grand progrès," a statement which history soon verified.

The method of adding the inoculum to melted gelatine and then pouring the mixture on a cooled glass plate was first published by Koch in 1883 and instantly found universal application the world over. The publication of this method was made in a most out of the way place viz. in a lecture at the 11th Deutschen Arztetag in Berlin 23rd June 1883, and published in the *Aerztliches Vereinsblatt für Deutschland*, No. 137. This paper is unknown in this country and I have been unable to see it in the original. Koch's lecture is however republished in his *Gesammelte Werke* (1912, Bd. i. p. 274) and the method will be found on page 280, as applied to the bacteriological examination of water. Apart from the substitution of agar for gelatine the only change in the Koch technique was that introduced in 1887 by Petri who poured the melted medium into three separate covered dishes—"Doppelschälchen" he called them. Petri described his method as "Ein kleine Modification des Koch'schen Plattenverfahrens" (*Centralbl. f. Bacteriol.*, 1887, i. 279), but it was destined to replace Koch's plates entirely and at once. Such in brief were the steps by which the methods of the pure cultivation of bacteria were perfected and by this means a revolution took place in our notions of ætiology in disease. In 1880 Koch himself worked out the causes of several traumatic infective diseases in animals. In 1882 he discovered the tubercle bacillus and in 1884 the cholera vibrio. In 1882 Loeffler and Schütz isolated the glanders

bacillus and in 1884 Gaffky the typhoid bacillus. In 1884 Loeffler isolated the diphtheria bacillus. The decade 1876-1886 was the heyday of bacteriological ætiological discovery as the decade 1886-1896 was the first great period of immunological research.

I have made a long digression from Klein and must now return to him in his lonely furrow in England. Although not hampered by lack of money or material and still a man in his prime he did not succeed in making a discovery comparable to those which were falling into the hands of Koch and his collaborators and it is tragic that he left no permanent impression on the literature of this early bacteriological period. Indeed it may seem almost paradoxical but in quite a number of instances he failed at first even to confirm work which has become established bacteriological knowledge. It would be a matter of interest to know precisely wherein Klein failed. Ehrlich used to be fond of saying that the successful prosecution of scientific work requires the possession of four "G's," viz. "Geld, Geschick, Geduld, und Glück." Klein lacked at least one of these requisites. Money it was not because he worked under the Government and was generously treated by it as far as cost of material went. He could always, for example, obtain cattle or sheep for experiments. It was not patience that was absent because Klein was a tremendously diligent plodder with an untiring industry. Between 1868 and 1910 he wrote not less than 264 separate papers and books, and of these not less than 200 on bacteriological subjects. For the Privy Council and Local Government Board alone he wrote close on 100 reports many of great length and full of experimental detail. A great deal of his work is buried away in Government reports and is largely lost. In looking through this mass of work in the last two months I have been struck with Klein's output and his perseverance. Klein had "Geschick" but I think there must have been some flaw in it. What it was I cannot say. There is some reason to suppose that in the early days he did not always keep abreast with the rapid progress that was being made. I have been informed that as late as 1885 he was attempting to cultivate the glanders bacillus in long capillary tubes but this method had been discarded years before. Klein probably arrived in the bacteriological field just a very few years too soon, and was not quite in a position to master the minute details necessary for successful bacteriological research. His fine histological technique did not suffice. In his later period he was, however, an exceedingly skilled bacteriological worker. We may assume that his luck was out as an original worker in the early days.

For his relative failure to make any really big discovery Klein was not altogether to blame. He was trained as a histologist but when he came to England he was largely under the influence of physiologists, who to put it plainly were dabbling in pathological matters. Other masters were medical officers of health who were tackling very difficult disease problems by methods quite insufficient at the time. Many of

Klein's early papers deal with things like sheep-pox, hog cholera, scarlet fever, foot-and-mouth disease, which even to-day are not altogether cleared up. He was also brought under the influence of what we, in this country, call epidemiologists. In Klein's day these were always suggesting some correlation between well-known human diseases and mysterious lesions on the teats of cows, and were following no doubt the Jennerian tradition in the hope of a new and greater discovery than cow-pox. A hundred years of study has shown that this has not been a fruitful line of inquiry except in Jenner's case. Klein in my judgment would have been more successful if he had been left to himself both with regard to the subjects of investigation as well as to the interpretation of the results. In some ways he was a bacteriologist *malgré lui*. I have looked through most of his work and am struck by its extraordinary range. Although the output was enormous there was almost always something in it. Thus I find him writing on variola (1874, 1879) enteric fever (1875-1902) scarlet fever (1876, 1885, 1893) swine fever (1877-1895) tubercle (1881) meat poisoning (1881-1890) anthrax (1883) jequirity ophthalmia (1884) cholera (1885-1896) foot-and-mouth disease (1885) pneumonia (1885) disinfection (1895-1910) fowl diarrhœa (1889) grouse disease (1889-1892) pheasant disease (1893-1902) diphtheria (1889-1890) immunity (1892-1902) oysters (1894-1905) psorosperms (1894) plague (1897-1906) bacillus enteritidis sporogenes (1895-1905) tubercle bacilli in milk (1900) rat bacilli (1901) and trypanosomes (1909). His first paper on the epithelium of the palate was in 1868 and his last in 1909, forty-one years later, on the action of boron preservatives on *Bacillus coli* and allied microbes.

Although it is true that Klein had not the good fortune to make a really important discovery in the causes of infective disease he exercised a profound and beneficial influence in England on the application of bacteriological science to the problems of public health, and may indeed be said to have founded and controlled this branch for nearly thirty years in a manner that was entirely to his credit. He was an individualised worker, and although he taught and disseminated bacteriological knowledge at St Bartholomew's Hospital and elsewhere he cannot be said to have established a school. With few exceptions he published his works under his own name only. It cannot serve a useful purpose to enter into details of all his successes and failures. He never slavishly copied the work of others; indeed he usually took a new line of his own and even if it proved incorrect he stuck to his opinions with great tenacity. Witness for example his prolonged opposition to Koch in connection with the comma bacillus, and his belief in the so-called Hendon disease, which on the opinion of W. H. Power was supposed to be scarlatina in the cow. In 1899 he expressed the opinion, now regarded as erroneous, that diphtheria in man was related in some mysterious way to cats. This was chiefly based on his

belief that diphtheria cultures produce a specific renal lesion in these animals. The lesion was a profound fatty infiltration of the cortex. It is now well known and indeed was well known long before Klein's time that this is almost a normal condition in town bred cats. He also strayed in his attempt to correlate human diphtheria with vesicular eruptions on the udders of cows. A great deal of his bacteriological work as applied to sanitary science was however correct and of permanent value.

Throughout his life in England Klein identified himself completely with his adopted country and was naturalised in 1887. All the memories of him will remain favourable. In early life he was described as unusually handsome and he remained very distinguished looking, tall and spare. Our portrait is a striking likeness of him about 1910. He spoke broken English to the end. Of affable austrian manners he was often dogmatic and on occasion polemical but took defeat in a thoroughly sportsmanlike fashion and bore no permanent grudges. In 1877 he was married in the English Church to Sophia Mawley by whom he had two daughters and a son. His domestic life was of the happiest kind. He lived for many years in the Earl's Court district and at the outbreak of war was at Chiselhurst in retirement. The war greatly upset him as he was thoroughly English in his outlook although his native country was warring against us. In 1921 he returned to London (61A Longridge Road, Earl's Court) but his health began to deteriorate from chronic bronchitis and in 1924 he went to live at Hove where he died from pneumonia. He was very musical and an adept at the chess table. He was often in his earlier years to be found playing his favourite game at Simpson's or in the British Chess Club, Covent Garden, where he took on a doughty champion like Blackburn. It is pleasing to know that in retirement he had few financial worries. He left £14,598.

WILLIAM BULLOCH.

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